IN THE CLAIMS

Please cancel claims 4, 8, 19 and 22 without prejudice or disclaimer.

Please add the following new claims 29-32.

This listing of the claims replaces all prior versions of the claims in the application.

1. (Currently Amended) An isolated polypeptide ~~comprising an amino acid sequence~~ selected from the group consisting of:

a) an polypeptide comprising an amino acid sequence ~~selected from the group consisting~~ of SEQ ID NO:[[1-]]11,

b) a polypeptide comprising a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence ~~selected from the group consisting~~ of SEQ ID NO:[[1-]]11, and

c) a biologically active fragment of a polypeptide comprising an amino acid sequence ~~selected from the group consisting~~ of SEQ ID NO:[[1-]]11~~, and~~

~~d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:[[1-]]11~~.

2. (Currently Amended) An isolated polypeptide of claim 1 ~~selected from the group consisting of~~ comprising SEQ ID NO:[[1-]]11.

3. (Original) An isolated polynucleotide encoding a polypeptide of claim 1.

4. (Canceled)

5. (Currently Amended) An isolated polynucleotide of claim 3 comprising ~~selected from the group consisting of~~ SEQ ID NO:[[12-]]22.

6. (Original) A recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide of claim 3.

7. (Original) A cell transformed with a recombinant polynucleotide of claim 6.

8. (Canceled)

9. (Original) A method for producing a polypeptide of claim 1, the method comprising:

a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide, and said recombinant polynucleotide comprises a promoter sequence operably linked to a polynucleotide encoding the polypeptide of claim 1, and

b) recovering the polypeptide so expressed.

10. (Original) An isolated antibody which specifically binds to a polypeptide of claim 1.

11. (Currently Amended) An isolated polynucleotide ~~comprising a polynucleotide sequence~~ selected from the group consisting of:

a) a polynucleotide comprising a polynucleotide sequence ~~selected from the group consisting~~ of SEQ ID NO:[[12-]]22,

b) a polynucleotide comprising a naturally occurring polynucleotide sequence having at least 70% sequence identity to a polynucleotide ~~sequence selected from the group consisting~~ of SEQ ID NO:[[12-]]22,

c) a polynucleotide ~~sequence~~ complementary to a),

d) a polynucleotide ~~sequence~~ complementary to b), and

e) an RNA equivalent of a)-d).

12. (Canceled)

13. (Original) A method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 11, the method comprising:

a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample,

and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide or fragments thereof, and

b) detecting the presence or absence of said hybridization complex, and, optionally, if present, the amount thereof.

14. (Canceled)

15. (Original) A method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 11, the method comprising:

a) amplifying said target polynucleotide or fragment thereof using polymerase chain reaction amplification, and

b) detecting the presence or absence of said amplified target polynucleotide or fragment thereof, and, optionally, if present, the amount thereof.

16. (Original) A composition comprising an effective amount of a polypeptide of claim 1 and a pharmaceutically acceptable excipient.

17. (Currently Amended) A composition of claim 16, wherein the polypeptide comprises an amino acid sequence ~~selected from the group consisting~~ of SEQ ID NO:[[1-]]11.

18-24. (Canceled)

25. (Original) A method of screening for a compound that specifically binds to the polypeptide of claim 1, said method comprising the steps of:

a) combining the polypeptide of claim 1 with at least one test compound under suitable conditions, and

b) detecting binding of the polypeptide of claim 1 to the test compound, thereby identifying a compound that specifically binds to the polypeptide of claim 1.

26. (Original) A method of screening for a compound that modulates the activity of the polypeptide of claim 1, said method comprising:

a) combining the polypeptide of claim 1 with at least one test compound under conditions permissive for the activity of the polypeptide of claim 1,

b) assessing the activity of the polypeptide of claim 1 in the presence of the test compound, and

c) comparing the activity of the polypeptide of claim 1 in the presence of the test compound with the activity of the polypeptide of claim 1 in the absence of the test compound, wherein a change in the activity of the polypeptide of claim 1 in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide of claim 1.

27. (Canceled)

28. (Original) A method for assessing toxicity of a test compound, said method comprising:

a) treating a biological sample containing nucleic acids with the test compound;

b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of a polynucleotide of claim 11 under conditions whereby a specific hybridization complex is formed between said probe and a target polynucleotide in the biological sample, said target polynucleotide comprising a polynucleotide sequence of a polynucleotide of claim 11 or fragment thereof;

c) quantifying the amount of hybridization complex; and

d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.

29. (New) A microarray wherein at least one element of the microarray is a polynucleotide of claim 3.

30. (New) A method of generating an expression profile of a sample which contains polynucleotides, the method comprising:

a) labeling the polynucleotides of the sample,

b) contacting the elements of the microarray of claim 29 with the labeled polynucleotides of the sample under conditions suitable for the formation of a hybridization complex, and

c) quantifying the expression of the polynucleotides in the sample.

31. (New) An isolated polynucleotide consisting of at least 60 contiguous nucleotides of a polynucleotide of claim 11.

32. (New) A method of screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence of claim 3, the method comprising:

a) exposing a sample comprising the target polynucleotide to a compound, under conditions suitable for the expression of the target polynucleotide,

b) detecting altered expression of the target polynucleotide, and

c) comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound.

REMARKS

I. Amendment to the Specification

The specification has been amended to add the priority information necessary to comply with 35 U.S.C. § 119(e) and 37 C.F.R. § 1.78. Applicants previously made a proper claim to priority under Article 8 of the Patent Cooperation Treaty (See pages 1-2 of the Declaration and Power of Attorney filed January 28, 2002).

II. Comments Regarding Restriction Requirement

Applicants hereby elect, with traverse, to prosecute Group 21, which corresponds to claims 3 and 5-7, 9, and 11.

A. The unity of invention standard *must* be applied in national stage applications

Section 1850 of the Manual of Patent Examining Procedure (original 8th edition, published August, 2001) (hereinafter "MPEP") provides:

> ... [W]hen the Office considers international applications ... during the national stage as a Designated or Elected Office under 35 U.S.C. 371, PCT Rule 13.1 and 13.2 will be followed when considering unity of invention of claims of different categories without regard to the practice in national applications filed under 35 U.S.C. 111....
>
> In applying PCT Rule 13.2 to ... national stage applications under 35 U.S.C. 371, examiners should consider for unity of invention all the claims to different categories of invention in the application and permit retention in the same application for searching and/or preliminary examination, claims to the categories which meet the requirements of PCT Rule 13.2....

Id at page 1800-60 to -61.

MPEP section 1893.03(d) reiterates the Examiner's obligation to apply the Unity of Invention standard PCT Rule 13.2 instead of U.S. restriction/election of species practice:

> Examiners are reminded that unity of invention (not restriction) practice is applicable ... in national stage (filed under 35 U.S.C. 371) applications.

Id at page 1800-149, column 1.

B. Specific provisions of the Administrative Regulations Under the PCT and the corresponding provisions of the MPEP strongly support a finding of unity of invention among all of the claims in the present case

1. Unity of Invention is accepted between claims to polypeptides and claims to the polynucleotides which encode them

Example 17, Part 2 of Annex B to the Administrative Instructions Under the PCT provides that unity of invention is accepted between a protein and the polynucleotide that encodes it:

> *Example 17*
> Claim 1: Protein X.
> Claim 2: DNA sequence encoding protein X.
> Expression of the DNA sequence in a host results in the production of a protein which is determined by the DNA sequence. The protein and the DNA sequence exhibit corresponding special technical features. Unity between claims 1 and 2 is accepted.

Applicants submit that claims drawn to the polypeptide sequence of SEQ ID NO:11 (*i.e.*, claims 1, 2, 16, and 17 of Group 11) and claims drawn to the elected polynucleotide sequence of SEQ ID NO:22, which encodes SEQ ID NO:11 (*i.e.*, claims 3, 5-7, and 9 of Group 21), meet the unity of invention requirements.

2. Unity of invention exists with respect to dependent claims in the same claim category as the independent claim from which they depend

MPEP section 1850(A) and 1893.03(d), which recite the provisions of paragraph (c) of Part 1 (entitled "Instructions Concerning Unity of Invention") of Annex B (entitled "Unity of Invention") to the Administrative Instructions Under the PCT, provides:

> **(A) Independent and Dependent Claims.**
>
> Unity of invention has to be considered in the first place only in relation to the independent claims in an international application and not the dependent claims. By "dependent" claim is meant a claim which contains all the features of another claim and is in the same category of claim as that other claim (the

> expression "category of claim" referring to the classification of claims according to the subject matter of the invention claimed for example, product, process, use or apparatus or means, etc.).
>
> (i) If the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of any claims that depend on the independent claims. In particular, **it does not matter if a dependent claim itself contains a further invention**.... (Emphasis added.)

See MPEP section 1850(A) at page 1800-61. See also MPEP Appendix AI at page 53.

Accordingly, claim 10, drawn to antibodies, should also be examined together with claim 1, drawn to the polypeptides from which claim 10 depends. Moreover, claims 2, 3, 5-7, 10, 16, and 17, all of which depend from claim 1, are all directed to compositions of matter, *i.e.,* to products. Further, as discussed above, there is unity of invention among claims 1 and 3.

3. Unity of invention exists among all of Applicants' claims

MPEP 1850 provides:

> Unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more special technical features. The term "special technical features" is defined as meaning those technical features that define a contribution which each of the inventions considered as a whole, makes over the prior art. The determination is made based on the contents of the claims as interpreted in light of the description and drawings. Annex B also contains examples concerning unity of invention.

Id at page 800-61.

MPEP 1893.03(d) similarly provides:

> A group of inventions is considered linked to form a single general inventive concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature. The expression special technical features is defined as meaning those technical features that define the contribution which each claimed invention, considered as a whole, makes over the prior art. For example, a corresponding technical feature is exemplified by a key defined by certain claimed structural characteristics which correspond to the claimed features of a lock to be used with the claimed key. Note also examples 1-17 of Annex B Part 2 of the PCT Administrative Instructions as amended July 1, 1992 contained in Appendix AI of the MPEP.

Id at page 1800-149.

In the present case, unity of invention exists among all of Applicants' claims. The sequences of the claimed polypeptides and the sequences of the claimed polynucleotides

encoding those polypeptides are corresponding technical features which are common to all of Applicants claims, which serve to technically interrelate all of Applicants' claims, and which define the contribution over the prior art made by each of them. Thus, Applicants' claims are linked to form a single general inventive concept, and Applicants are therefore entitled to prosecute all of their pending claims in a single national stage application.

4. The sequences of the claimed polypeptides and the claimed polynucleotides encoding those polypeptides, are corresponding technical features that are common to all of Applicants' claims and that serve to technically interrelate them

The sequences of the claimed polypeptides and corresponding polynucleotides are common to all of Applicants' claims, given that each claim refers to one or both either explicitly or implicitly, by virtue of depending from a claim which makes an explicit reference to the sequences of the claimed polypeptides or claimed polynucleotides.

Moreover, the sequences of the claimed polypeptides and corresponding polynucleotides serve to technically interrelate all of Applicants' claims. Applicants' composition of matter claims 1-3, 5-7, 10, 11, 16, 17, and 31) are drawn to either the polypeptides or polynucleotides themselves (1 and 2, drawn to polypeptides, and 3, 5 and 11, drawn to polynucleotides), to compositions of matter which comprise the polypeptides or polynucleotides as one element (6 and 7, drawn to recombinant polynucleotides and transformed cells, respectively, and 16 and 17, drawn to pharmaceutical compositions), or to compositions of matter wherein the sequences of the claimed polypeptides functionally limit the claimed subject matter (Claim 10, drawn to an antibody which specifically binds a polypeptide of claim 1).

In Applicants' method claims 9, 13, 15, 25, 26, and 28), the claimed polypeptides or polynucleotides serve as either the product of the claimed method (claim 9, drawn to a method of polypeptide production) and/or as a reagent for performing the method (claims 13 and 15 drawn to methods of detecting a target polynucleotide in a sample; claim 25, drawn to a method of screening for a compound that specifically binds to a polypeptide of claim 1; claim 32, drawn to a method of screening a compound for effectiveness in altering expression of a polynucleotide of claim 3; and claim 28, drawn to a method of assessing toxicity of a test compound using a polynucleotide of claim 11).

Therefore, the sequences of the claimed polypeptides and polynucleotides are

corresponding technical features which are common to all of Applicants' claims, and which serve to technically interrelate them.

5. Minimal burden to search claims 13, 15, and 28-32, under U.S. practice

Applicants also respectfully submit that the search required to identify prior art relevant to the polynucleotides of claim 31 should substantially overlap with that required for examination of the elected polynucleotides of Group 21. In addition, there is minimal additional burden on the Examiner to examine claims 13 and 15 (Group 54), claim 28 (Group 86) and newly added claim 32, which is drawn to methods of using the elected polynucleotides, and newly added claims 29 and 30, which are drawn to microarrays using the elected polynucleotides.

III. Rejoinder of method claims upon allowance of product claims under U.S. practice

The Examiner is reminded that claims 13 and 15 (Group 54), 28 (Group 86) and 32 drawn to methods of using the elected polynucleotides of Group 11 should be rejoined per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," which sets forth the rules that upon allowance of any of the product claims, the method claims covering the same scope of products be rejoined. Applicants request that claims 13 and 15 (Group 54), 28 (Group 86) and 32 be rejoined and examined upon allowance of any claim drawn to the claimed polynucleotides.

It is noted that, while Applicants have canceled and not repeated new versions of the claims of Group 32, drawn to a transgenic organism and Group 64, drawn to agonists and antagonists. Applicants expressly assert that these claims have been canceled for reasons relating to cost and efficiency of prosecution of the presently elected claims, and not for reasons relating to patentability. Applicants further expressly reserve the right to pursue the subject matter of those canceled claims, or any other subject matter disclosed but not herein claimed, in a later continuation or divisional application.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding objections/rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned at the number listed below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,

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